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EDITORIAL

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful. The editor, alone, is responsible for their type, their tone and their tenor.

THE POSITION OF PHARMACY IN PUBLIC HEALTH

PHARMACY'S history is one of its proudest assets, for "the art of the apothecary" has been practiced since the first man had his first illness. Thus, when our ancestors fell heir to, or chose their duties, some of them, by nature or by inclination, came into the practice of medicine and pharmacy.

Through many centuries, the two professions, were interdependent and inseparable. In most instances medicine and pharmacy were practiced simultaneously by the same individuals. Then, in the twelfth and thirteenth centuries, further delineation of communal duties brought about the establishment of apothecary shops, or drug stores, owned and managed by men whose specialized work as pharmacists demanded so much of their time that they could not enter also into the practice of medicine.

Today we find the same distinction of duties, together with harmony and understanding between the professions of medicine and pharmacy, each, in its own way and with the assistance of the other, playing its part in the never ending struggle against pain, sickness and disease. Dentistry, nursing and the other public health services are indispensable allies in this united endeavor to bring about longer and healthier lives. It has been a progressive battle. In a period of only a century and a half in this country, man's life expectancy has risen from 35 to 62 years. The products provided by modern pharmacy have contributed in no small measure to this result.

The Meaning of the Profession

Pharmacy is the art and science of preparing from natural and synthetic sources suitable and convenient materials for use as drugs. It also comprehends the compounding of drugs and the dispensing of drugs and medicines according to prescription, and their distribution in other ways. Pharmacy also embraces the collection, identification,

preservation, analysis and standardization of drugs and medicines; the synthesis of medicinal chemicals and the preparation of biological products. In short, the primary function of pharmacy is to prepare medicines for those who need them.

Pharmacy's Progress

From its domination in early days by alchemy and superstition, pharmacy has developed into a highly specialized art involving the application of the exact and exacting sciences. The necessity of trade has always been a more or less important factor in its existence, and has, at times, seemed to obscure its real value and function. Yet, through a happy fellowship of professionalism and commercialism, the ready availability and distribution of drugs and medicines throughout this country is provided for. In the United States there are a sufficient number of adequately trained registered pharmacists. One hundred and twenty thousand of these professional and scientific workers, practicing in 60,000 registered pharmacies, and 3000 hospitals, insure that no person is at any time very far removed from an adequate and reliable source of medicaments.

Based on the country's population, this indicates one drug store ready to serve each 2000 people. In the aggregate, 200,000,000 prescriptions are filled by these pharmacists each year. Hospital and clinic pharmacies fill countless others.

The Pharmacist Serves the Public Welfare

In addition to the compounding of prescriptions, retail pharmacists in drug stores render many other useful services. Through the knowledge which they have gained in years spent in colleges of pharmacy in their apprenticeships and in their practice, they make a special contribution to the welfare of the citizen. Their intelligence in the methods of preparing and properly combining medicinal substances places them constantly in a position to assist practicing physicians in the successful treatment of disease. They likewise supply physicians and dentists with sterile solutions, antiseptics, surgical aids, anesthetics, stains used in the study of bacteria; also various other materials used in diagnosis and treatment.

The retail pharmacist is also a frequent source of supply for veterinary medicines, insecticides, fungicides, rodent poisons, household disinfectants and many similar articles with which he has become so familiar.

Serums, and vaccines, foods for infants and invalids, sickroom and first-aid supplies, and sanitation aids are customarily distributed by pharmacists because of the specialized knowledge required for the preparation, storage and use of these items.

The retail or hospital pharmacist frequently manufactures such compounds as must be freshly prepared, and he also manufactures a number of medicines which can be economically prepared in his own laboratory. He is also the center of distribution and the focal point of information and advice concerning the myriad of vital preparations manufactured in the great, centrally located laboratories.

And here we have a modern phase of pharmacy, to the casual onlooker little known, because part of the practice of the profession has passed from the hands of the "apothecary" into other yet capable hands. The extensive drug industry—huge drug collecting organizations and milling concerns, large manufacturers of organic and inorganic chemicals of medical value, immense pharmaceutical manufacturing establishments, biologic laboratories, institutes of pharmaceutic research—all of these are integral parts of the pharmacy of today, with the corner Drug Store an important link in the chain of agencies necessary to provide all the preparations required by modern medicine. As the actual prescription-compounding, medicine-supplying station, the corner drug store, notwithstanding its side lines, is a valuable, serviceable spot in every community.

The Pharmacist in the Community

As a general rule, pharmacists are intensely civic-minded. They are often active in various service clubs, chambers of commerce, church and charity organizations, and other groups working for the betterment of the community. Often, their stores are the centers of neighborhood activity along these lines. Open for a greater part of the day than most business establishments, they lend themselves admirably to this purpose.

The Law Recognizes the Pharmacist

Recognized as a public health profession in every civilized country in the world, the practice of pharmacy in all such countries is regulated by law. In the United States the laws of the various States limit the practice of pharmacy to those who are properly qualified and licensed as determined by formal collegiate education and subsequent state governmental examination. These same laws have placed the

legal distribution of poisons, potent drugs and medicines and narcotics under the supervision of pharmacists.

Such laws are just, and work for public benefit. Under these regulations, pharmacy is able to render an incomparable service to the community. If the public interest be given full consideration there should be no curtailment of the services now rendered by the pharmacists of the nation. Obviously, therefore, any effort in the direction of concentrating pharmaceutical facilities in governmental departments or health centers except in a few very special cases, would reduce the availability of adequate assistance on a private scale. Pharmacy is a profession of service to each citizen in each country. It must and will always be so.

Your Pharmacist Greets You

Whether you are well, or whether you are ill, your pharmacist greets you. He is eminently prepared to render professional service without limit. He is happy and willing to render the multitude of other services you are accustomed to expect of your favorite pharmacy.

Your pharmacist is your friend.

Effect of Radiant Energy on Thermophilic Organisms in Sugar. H. H. Hall and J. C. Keane. *J. Ind. & Eng. Chem. 31,* 1168 (1939). Results obtained by the Bureau of Agricultural Chemistry indicate that the spores of a thermophilic organism which spoils canned food, *B. stearothermophilus* Donk, are killed in dry white sugar by radiant energy rays most of which are in the region 253.7 μ. The lethal action is enhanced when the sugar crystals are kept in constant motion in the sugar granulator during irradiation. For this purpose, 24 thirty inch lamps were installed in the sugar outlet end of a granulator. Under these conditions an average of 47.8 per cent. of the spores were killed by irradiating eight successive batches of sugar. No chemical changes were noted in the irradiated product. The results indicate the possibility of sterilizing sugar and other such substances by this method.

L. F. T.

ORIGINAL ARTICLES

A NEW APPROACH TO THE STANDARDIZATION OF DIGITALIS

By Arno Viehoever, N. H. Sokoloff and A. A.Taransky * †

I. Introduction

THE unsolved problem of devising a reliable method for the standardization of digitalis and its preparations has been intensively investigated for several decades. Although it is agreed that graded dosage of this important heart tonic can be permitted only by standardization, the majority of methods devised for measuring potency are in reality merely toxicity assays. Were it true that the toxicity of a digitalis preparation is related to its therapeutic efficiency in correcting cardiac dysfunction, then such methods for the assay of potency would have a logical basis. However, we believe that potency in the case of digitalis can scarcely be considered as synonymous with toxicity. Thus, the official methods of standardization are toxicity assays which indicate the margin of safety of a preparation and not the actual therapeutic value.

Significant discrepancies in results have been reported by different workers using the same methods for a single sample of digitalis, and with the use of other methods the disagreement has been more marked. Even in the case of the U. S. P. XI Digitalis Standard, Rowe has reported that there is a variable action, and that it is 50 per cent. stronger than the U. S. P. X Standard (8).

The senior author and his previous students (5 and 6) had studied the effect of digitalis and certain of its constituents upon the heart of Daphnia magna. Digitoxin rapidly depressed the rate of heartbeat. Also, as recorded in micromovies (7), the spastic heartbeat of daphnia produced by chloroform was abolished, and a regular rhythm with increased force established through the use of digitalis and Verodigen—a preparation of digitalis glucosides. More recent studies have disclosed the fact that certain types of drug-induced depression of the rate of heartbeat could be wholly or partially prevented

* From the Gross Laboratory for Biological and Biochemical Research.

† We are indebted to Dr. Isadore Cohen for invaluable aid and advice in these experiments.

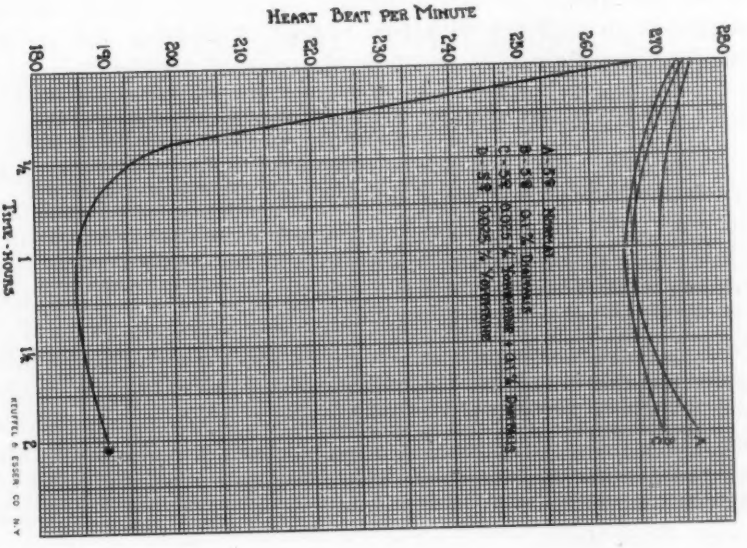
in the presence of an active digitalis preparation. These findings suggested an approach to a new method of studying and perhaps standardizing digitalis by its desirable remedial activity.

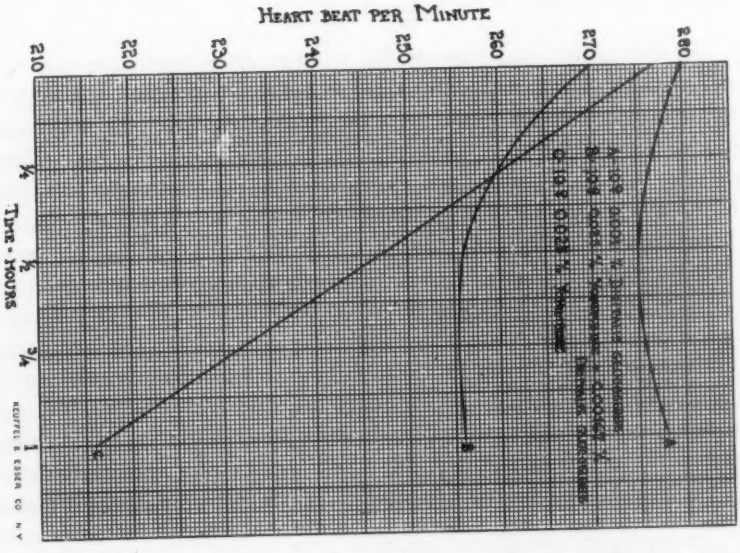
II. Description and Culture of Daphnia Magna

Daphnia magna is a small (1/10 inch) transparent, fresh-water crustacean belonging to the Cladocera. It possesses well developed muscular, nervous and glandular systems. The ease of observation of the internal organs functioning normally and under drug or toxic action permits direct quantitative measurements (3). The propagation of Daphnia magna has been reported by Viehoever (1) and the methods of standardization by Viehoever and Cohen (4). Cultured under uniform conditions, Daphnia magna exhibits a definite rhythm and periodicity of growth. Reproduction is chiefly through diploid parthenogenesis. Numerous offspring of genetical uniformity is thus assured for statistical studies. The offspring can reproduce in ten days, while the life span of the species at 70 degrees F. is approximately ninety days.

III. Description of the Methods Used in the Daphnia Experiments

In the earlier experiments the hanging-drop technique was utilized. Double depression slides were found to be especially satisfactory since a control animal could be mounted for direct comparison with the test animal which was suspended in the drug mixture. These mixtures consisted either of yohimbine (2), veratrine or atropine which depress the rate of heartbeat of daphnia, and digitalis or digitalis glucosides in varying proportions. Although this method possessed the virtue of simplicity, there were numerous disadvantages and sources of errors. The amount of the test solution was limited to a single drop, and there was an unavoidable variation in the size of the drop from one experiment to another. The cooling effect of evaporation caused a decrease in the rate of heartbeat, and furthermore, the condensation of the water vapor produced a blurred image which interfered with the observations. In addition, the consequent reduction of the oxygen-tension level appeared to impair the respiratory function of the test animals, and this undoubtedly contributed in many cases to the recording of abnormally low levels of depression in rate of heartbeat.


Heart Beat per Minute
180
190
200
210
220
230
240
250
260
270
280
¼
Time - Hours
1
1¼
1½
2
A
B
C
D
KEUFFEL & ESSER CO N.Y


Heart beat per Minute
210
220
230
240
250
260
270
280
¼
Time - Hours
½
¾
1
A
B
C
KEUFFEL & ESSER CO N.Y

Small double chambers were used and soon abandoned in favor of the following method and its variation. Although the double chamber could be used to project a normal and a test animal simultaneously, the technique involved in mounting the animals was too time consuming and possessed several of the disadvantages of the hanging-drop method.

The procedure, designated by us as the Mass Culture method, has demonstrated its merit. Daphnia from a standardized culture are divided into two groups. The first is placed in a one ounce bottle three-quarters filled with the drug solution which depressed the rate of heartbeat, and the second group is placed in a bottle similarly filled with a mixture of the depressant drug and digitalis or digitalis glucosides in varying proportions. At uniformly timed intervals the daphnia were rapidly removed, and the rate of heartbeat was determined in the depression of a ground glass slide. The protective activity of digitalis was manifested at that concentration where none or little depressant activity was observed in the mixture of depressant drug and digitalis. The level of depression caused by the depressant activity of the drug was obtained in the first group, and intermediate levels were obtained in certain concentrations of the drug and digitalis mixtures. Of course, the normal rate of hearbeat was determined at the beginning of the assay, and precautions were taken to maintain a constant temperature, usually 70 degrees F., at which temperature it has been our practice to culture the daphnia.

A variation of this method, designated as the Single Culture method, consists of the taking the normal heartbeats of many daphnia and placing them individually in the one ounce bottles similarly filled with the depressant drug and mixtures of the depressant drug and digitalis in various concentrations. In this way, the reactions of individual daphnia could be studied over long periods of time. The rate of heartbeat was counted as in the immediately preceding method. This Single Culture method can be employed after the injection of definite amounts of drug and drug-digitalis mixtures, and culture medium is used in their stead in the bottles. In this paper we shall report only those results which do not embody the microinjection technique.

IV. Results and Discussion

Yohimbine, because of its relatively low toxicity, was found to be the most suitable cardiac depressant for our purposes. Degree of

cardiac depression in daphnia is measured by the decrease in the number of heartbeats per minute. Three samples of digitalis were used: Powdered Digitalis Leaf (A), International Standard Digitalis (B), and a mixture of Digitalis glucosides (C).

Five daphnia (Table I) placed in 0.025 per cent. yohimbine solution, and having an average normal heartbeat of 267, at the end of two hours had an average heartbeat of only 190. On the other hand, the five daphnia which were placed in mixture of 0.025 per cent. yohimbine

TABLE II

EFFECT OF DIGITALIS LEAF PREPARATIONS AGAINST YOHIMBINE DEPRESSION

Normal Heart Beat	Normal Heart Beat	Normal Heart Beat
1. 281 hrt. bts. /min.	1. 283 hrt. bts. /min.	1. 273 hrt. bts. /min.
2. 287 " " "	2. 292 " " "	2. 285 " " "
3. 300 " " "	3. 292 " " "	3. 277 " " "
4. 283 " " "	4. 269 " " "	4. 269 " " "
5. 290 " " "	5. 274 " " "	5. 277 " " "
Av. 288	Av. 282	Av. 276

One Hour

.025% Yohimbine	.025% Yohimbine + .0745% Dig. (A) *	.025% Yohimbine + .0345% Dig. (A)
1. 202 hrt. bts. /min.	1. 198 hrt. bts. /min.	1. 208 hrt. bts. /min.
2. 263 " " "	2. 214 " " "	2. 205 " " "
3. 225 " " "	3. 222 " " "	3. 217 " " "
4. 214 " " "	4. 243 " " "	4. 191 " " "
5. 209 " " "	5. 273 " " "	5. 209 " " "
Av. 223	Av. 190	Av. 206

Two Hours

.025% Yohimbine	.025% Yohimbine + .0745% Dig. (A) *	.025% Yohimbine + .0345% Dig. (A)
1. 181 hrt. bts. /min.	1. 185 hrt. bts. /min.	1. 180 hrt. bts. /min.
2. 157 " " "	2. 191 " " "	2. 164 " " "
3. 209 " " "	3. 157 " " "	3. 157 " " "
4. 167 " " "	4. 177 " " "	4. 151 " " "
5. 166 " " "	5. 195 " " "	5. 183 " " "
Av. 198	Av. 187	Av. 167

* This sample of Digitalis was bought on the open market. It was more than *two years* old and was kept without precautions to prevent deterioration.

TABLE I

PROTECTIVE EFFECT OF DIGITALIS LEAF PREPARATIONS OVER A WIDE RANGE AGAINST YOHIMBINE DEPRESSION

Single Culture Method

Normal Heart Beat	Normal Heart Beat	Normal Heart Beat	Normal Heart Beat	Normal Heart Beat	Normal Heart Beat	Normal He
1. 273 hrt. bts. /min.	1. 269 hrt bts. /min.	1. 275 hrt. bts. /min.	1. 292 hrt. bts. /min.	1. 277 hrt. bts. /min.	1. 277 hrt. bts. /min.	1. 295 hrt. b
2. 273 " " "	2. 257 " " "	2. 285 " " "	2. 269 " " "	2. 281 " " "	2. 269 " " "	2. 290 "
3. 253 " " "	3. 275 " " "	3. 271 " " "	3. 267 " " "	3. 273 " " "	3. 265 " " "	3. 288 "
4. 273 " " "	4. 250 " " "	4. 269 " " "	4. 269 " " "	4. 279 " " "	4. 277 " " "	4. 293 "
5. 300 " " "	5. 283 " " "	5. 277 " " "	5. 267 " " "	5. 285 " " "	5. 277 " " "	5. 295 "
Av. 274	Av. 267	Av. 275	Av. 273	Av. 278	Av. 273	Av. 292

One Hour

Normal Heart Beat	.025% Yohimbine	0.1% Digitalis (A)	.025% Yohimbine + 0.1% Digitalis (A)	.025% Yohimbine + .05% Digitalis (A)	.025% Yohimbine + .025% Digitalis (A)	.025% Yohi .0125% Digit
1. 259 hrt. bts. /min.	1. 228 hrt. bts. /min.	1. 265 hrt. bts. /min.	1. 290 hrt. bts. /min.	1. 245 hrt. bts. /min.	1. 247 hrt. bts. /min.	1. 272 hrt. b
2. 269 " " "	2. 188 " " "	2. 271 " " "	2. 240 " " "	2. 279 " " "	2. 272 " " "	2. 273 "
3. 255 " " "	3. 173 " " "	3. 265 " " "	3. 285 " " "	3. 269 " " "	3. 261 " " "	3. 275 "
4. 269 " " "	4. 172 " " "	4. 283 " " "	4. 269 " " "	4 257 " " "	4. 265 " " "	4. 281 "
5. 290 " " "	5. 172 " " "	5. 269 " " "	5. 240 " " "	5. 269 " " "	5. 273 " " "	5. 281 "
Av. 266	Av. 186	Av. 270	Av. 265	Av. 264	Av. 264	Av. 276

Two Hours

Normal Heart Beat	.025% Yohimbine	0.1% Digitalis (A)	.025% Yohimbine + 0.1% Digitalis (A)	.025% Yohimbine + .05% Digitalis (A)	.025% Yohimbine + .025% Digitalis (A)	.025% Yohi .0125% Digit
1. 223 hrt. bts. /min.	1. 200 hrt. bts. /min.	1. 269 hrt. bts. /min.	1. 269 hrt. bts. /min.	1. 240 hrt. bts. /min.	1. 263 hrt. bts. /min.	1. 271 hrt. b
2. 248 " " "	2. 148 " " "	2. 273 " " "	2. 273 " " "	2. 285 " " "	2. 272 " " "	2. 273 "
3. 281 " " "	3. 250 " " "	3. 273 " " "	3. 273 " " "	3. 277 " " "	3. 277 " " "	3. 269 "
4. 288 " " "	4. 175 " " "	4. 277 " " "	4. 277 " " "	4. 277 " " "	4. 257 " " "	4. 275 "
5. 285 " " "	5. 180 " " "	5. 261 " " "	5. 261 " " "	5. 273 " " "	5. 269 " " "	5. 277 "
Av. 275	Av. 190	Av. 270	Av. 270	Av. 270	Av. 268	Av. 273

TABLE I

LIS LEAF PREPARATIONS OVER A WIDE RANGE AGAINST YOHIMBINE DEPRESSION

Single Culture Method

Normal Heart Beat	Normal Heart Beat	Normal Heart Beat	Normal Heart Be
1. 292 hrt. bts. /min.	1. 277 hrt. bts. /min.	1. 277 hrt. bts. /min.	1. 295 hrt. bts. /n
2. 269 " " "	2. 281 " " "	2. 269 " " "	2. 290 " "
3. 267 " " "	3. 273 " " "	3. 265 " " "	3. 288 " "
4. 269 " " "	4. 279 " " "	4. 277 " " "	4. 293 " "
5. 267 " " "	5. 285 " " "	5. 277 " " "	5. 295 " "
Av. 273	Av. 278	Av. 273	Av. 292

One Hour

.025% Yohimbine + 0.1% Digitalis (A)	.025% Yohimbine + .05% Digitalis (A)	.025% Yohimbine + .025% Digitalis (A)	.025% Yohimbine .0125% Digitalis (
1. 290 hrt. bts. /min.	1. 245 hrt. bts. /min.	1. 247 hrt. bts. /min.	1. 272 hrt. bts. /n
2. 240 " " "	2. 279 " " "	2. 272 " " "	2. 273 " "
3. 285 " " "	3. 269 " " "	3. 261 " " "	3. 275 " "
4. 269 " " "	4 257 " " "	4. 265 " " "	4. 281 " "
5. 240 " " "	5. 269 " " "	5. 273 " " "	5. 281 " "
Av. 265	Av. 264	Av. 264	Av. 276

Two Hours

.025% Yohimbine + 0.1% Digitalis (A)	.025% Yohimbine + .05% Digitalis (A)	.025% Yohimbine + .025% Digitalis (A)	.025% Yohimbine .0125% Digitalis (
1. 269 hrt. bts. /min.	1. 240 hrt. bts. /min.	1. 263 hrt. bts. /min.	1. 271 hrt. bts. /n
2. 273 " " "	2. 285 " " "	2. 272 " " "	2. 273 " "
3. 273 " " "	3. 277 " " "	3. 277 " " "	3. 269 " "
4. 277 " " "	4. 277 " " "	4. 257 " " "	4. 275 " "
5. 261 " " "	5. 273 " " "	5. 269 " " "	5. 277 " "
Av. 270	Av. 270	Av. 268	Av. 273

rt Beat	Normal Heart Beat
s. /min.	1. 288 hrt. bts. /min.
" "	2. 277 " " "
" "	3. 283 " " "
" "	4. 277 " " "
" "	5. 288 " " "
	Av. 280

nbine + alis (A)	.025% Yohimbine + .00625% Digitalis (A)
ts. /min.	1. 274 hrt. bts. /min.
" "	2. 277 " " "
" "	3. 281 " " "
" "	4. 269 " " "
" "	5. 250 " " "
	Av. 270

nbine + alis (A)	.025% Yohimbine + .00625% Digitalis (A)
ts. /min.	1. 281 hrt. bts. /min.
" "	2. 277 " " "
" "	3. 281 " " "
" "	4. 273 " " "
" "	5. 269 " " "
	Av. 276

and 0.1 per cent. digitalis (A), and which had an average normal heartbeat of 273, at the end of two hours had an average heartbeat of 270, a decrease of only three beats. Five other animals which were kept in culture water instead of drug solution showed a variation in average heartbeat during the two hours which was essentially the same as in the yohimbine digitalis mixture. A solution of 0.1 per cent. digitalis (A) without yohimbine produced a depression of seven beats

TABLE III

EFFECT OF INTERNATIONAL STANDARD DIGITALIS AGAINST YOHIMBINE DEPRESSION

Normal Heart Beat	Normal Heart Beat	Normal Heart Beat
1. 270 hrt. bts. /min.	1. 290 hrt. bts. /min.	1. 277 hrt. bts. /min.
2. 295 " " "	2. 295 " " "	2. 285 " " "
3. 285 " " "	3. 285 " " "	3. 288 " " "
4. 272 " " "	4. 285 " " "	4. 279 " " "
5. 290 " " "	5. 300 " " "	5. 288 " " "
Av. 282	Av. 278	Av. 283
One Hour		
.025% Yohimbine	.025% Yohimbine + .0745% Dig. (B) *	.025% Yohimbine + .035% Dig. (B)
1. 225 hrt. bts. /min.	1. 212 hrt. bts. /min.	1. 231 hrt. bts. /min.
2. 247 " " "	2. 269 " " "	2. 235 " " "
3. 225 " " "	3. 176 " " "	3. 220 " " "
4. 212 " " "	4. 196 " " "	4. 192 " " "
5. 218 " " "	5. 222 " " "	5. 228 " " "
Av. 225	Av. 215	Av. 223
Two Hours		
.025% Yohimbine	.025% Yohimbine + .0745% Dig. (B) *	.025% Yohimbine + .035% Dig. (B)
1. 231 hrt. bts. /min.	1. 203 hrt. bts. /min.	1. 228 hrt. bts. /min.
2. 200 " " "	2. 214 " " "	2. 217 " " "
3. 189 " " "	3. 247 " " "	3. 214 " " "
4. 207 " " "	4. 219 " " "	4. 217 " " "
5. 180 " " "	5. 219 " " "	5. 218 " " "
Av. 201	Av. 220	Av. 219

* .0745% International Standard Digitalis solution is equivalent to one Cat Unit per 100 cc.

in the average heartbeat per minute, a depression which does not exceed the normal variation.

The protective action of digitalis (A) against 0.025 per cent. yohimbine was evident in concentrations as low as 0.0625 per cent.

A sample of the same preparation of digitalis, which was more than two years old and which had been kept with no precautions to prevent deterioration, exhibited no protective action. As a matter of fact, it seemed to augment rather than inhibit the action of yohimbine (Table II).

A smaller concentration of digitalis produced a corresponding decrease of protection (Table I). A concentration of 0.1 per cent. digitalis (A) allowed only a 5 per cent. depression; 0.00625 per cent. digitalis (A) allowed a depression of 11 per cent. This effect of graded dosage indicates the feasibility of using the protective action of digitalis as a basis for an assay.

More experiments by the Mass Culture method were carried out using 0.025 per cent. yohimbine and varying concentrations of digitalis glucosides. Ten animals, having an average normal heartbeat of 277, were placed in a 0.025 per cent. yohimbine solution. Ten other animals, whose average heartbeat was 270, were placed in a solution containing 0.025 per cent. yohimbine and 0.00167 per cent. digitalis glucosides. At the end of one hour the daphnia were removed one by one and their heartbeat counted and averaged. The first group had an average heartbeat of 216 and the group in the yohimbine-glucoside solution had dropped to 256 (Table IV). The time limit was set as one hour because the one hour and two hour readings were practically the same.

The protective action of digitalis glucosides (C) against 0.025 per cent. yohimbine was evident in a concentration as low as 0.00033 per cent.

Direct comparison can be made between samples (A) and (B) because they are both powdered leaf preparations. However, precise comparison of the protective action cannot be made between the powdered leaf preparations and digitalis (C), the glucosidal mixture, because of various other substances in the leaf preparations, which may directly or indirectly inhibit or augment the action of the cardiac glucosides present.

The results indicate that Digitalis (A) has a greater protective action than digitalis (B) at equivalent concentrations (Tables I and III). On the other hand digitalis (C) protects against 0.025 per

TABLE IV

PROTECTIVE EFFECT OF DIGITALIS GLUCOSIDES AGAINST YOHIMBINE DEPRESSION

Mass Culture

Normal Heart Beat	Normal Heart Beat	Normal Heart Beat
286 Beats per min.	274 Beats per min.	286 Beats per min.
269 " " "	281 " " "	269 " " "
279 " " "	267 " " "	271 " " "
270 " " "	293 " " "	276 " " "
280 " " "	287 " " "	268 " " "
281 " " "	278 " " "	263 " " "
263 " " "	280 " " "	268 " " "
277 " " "	265 " " "	263 " " "
279 " " "	288 " " "	269 " " "
269 " " "	288 " " "	267 " " "
277 Av. beats per min.	280 Av. beats per min.	270 Av. beats per min.

One-half Hour

0.025% Yohimbine HCl	0.0011% Digitalis Glucosides	0.025% Yohimbine HCl + 0.00167% Digitalis Glucosides
246 Beats per min.	286 Beats per min.	247 Beats per min.
249 " " "	276 " " "	261 " " "
255 " " "	263 " " "	266 " " "
257 " " "	272 " " "	282 " " "
297 " " "	276 " " "	267 " " "
287 " " "	265 " " "	250 " " "
213 " " "	284 " " "	286 " " "
239 " " "	276 " " "	285 " " "
252 " " "	274 " " "	257 " " "
264 " " "	274 " " "	245 " " "
247 Av. beats per min.	275 Av. beats per min.	256 Av. beats per min.

One Hour

0.025% Yohimbine HCl	0.0011% Digitalis Glucosides	0.025% Yohimbine HCl + 0.00167% Digitalis Glucosides
215 Beats per min.	275 Beats per min.	278 Beats per min.
216 " " "	268 " " "	248 " " "
232 " " "	281 " " "	246 " " "
218 " " "	286 " " "	260 " " "
228 " " "	274 " " "	248 " " "
224 " " "	273 " " "	252 " " "
166 " " "	266 " " "	242 " " "
237 " " "	279 " " "	260 " " "
213 " " "	284 " " "	257 " " "
213 " " "	272 " " "	269 " " "
216 Av. beats per min.	278 Av. beats per min.	256 Av. beats per min.

cent. yohimbine in a concentration of about 1/20 of that of digitalis (A). But as mentioned above no really direct comparison can be made (Table V).

Before this non-toxic method of assay can become feasible, a number of factors producing variation in results must be further investigated and brought under control. The animals must be of the same age, sex, and of the same vitality. Animals which are anemic, small and generally sluggish will not produce the same results as healthier animals. The temperature must be constant.

Most important of all, a better understanding of standardization of the daphnia cultures must be obtained. At the present time, digitalis of a definite concentration does not always exhibit the same degree of protection in experiments in which all other factors apparently do not vary. Likewise, yohimbine in the concentrations used in these experiments does not always exhibit the same degree of depression. Thus, there are two variables which may be eliminated with the use of daphnia from more precisely controlled cultures.

V. Conclusions

1. Digitalis leaf exhibits protective action on the heart of Daphnia magna against depressants (e. g. yohimbine). The degree of protection appears to be directly proportional to the amount of digitalis.

2. Mixtures of digitalis glucosides exhibit the same protective action.

3. Further work is necessary to fully explore the feasibility of this method for assay purposes.

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This work was carried on with the support and cooperation of Mr. J. Rosin, of Merck & Co.; the Sandoz Chemical Co., and John Wyeth & Bro., Inc.

TABLE V

Average Rate of Heart Beat Indicating Effect of Graded Dosage

Averages Obtained From Twenty-five Experiments Using Digitalis (A)

Normal Heart Beat per Min.	282	281	275	282	278	279	274	281
Dosage	0.025% Yohimbine	0.025% Yoh. + 0.1% Digitalis	0.025% Yoh. + 0.075% Digitalis	0.025% Yoh. + 0.05% Digitalis	0.025% Yoh. + 0.025% Digitalis	0.025% Yoh. + 0.0125% Digitalis	0.025% Yoh. + 0.00625% Digitalis	0.025% Yoh. + 0.003125% Digitalis
Heart Beat after 2 Hours	209	266	266	256	244	258	244	198

Fig. 1

Averages Obtained From Fifteen Experiments Using Digitalis (B)

Normal Heart Beat per Min.	274	288	280	273	275	276
Dosage	0.025% Yohimbine	0.025% Yoh. + 0.1% Digitalis	0.025% Yoh. + 0.0745% Digitalis	0.025% Yoh. + 0.05% Digitalis	0.025% Yoh. + 0.0345% Digitalis	0.025% Yoh. + 0.025% Digitalis
Heart Beat after 2 Hours	196	239	220	223	204	180

Fig. 2

Averages Obtained From Thirteen Experiments Using Digitalis (C)

Normal Heart Beat per Min.	276	280	272	279	270	271	272
Dosage	0.025% Yohimbine	0.025% Yoh. + 0.0033% Dig. Gluc.	0.025% Yoh. + 0.00165% Dig. Gluc.	0.025% Yoh. + 0.0011% Dig. Gluc.	0.025% Yoh. + 0.00066% Dig. Gluc.	0.025% Yoh. + 0.00033% Dig. Gluc.	0.025% Yoh. + 0.000165% Dig. Gluc.
Heart Beat after 1 Hour	188	242	244	252	240	220	199

Fig. 3

EFFECT OF GRADED DOSAGE

iments Using Digitalis (A)

278	279	274	281
0.025% Yoh. + 0.025% Digitalis	0.025% Yoh. + 0.0125% Digitalis	0.025% Yoh. + 0.00625% Digitalis	0.025% Yoh. + 0.003125% Digitalis
244	258	244	198

ents Using Digitalis (B)

273	275	276
0.025% Yoh. + 0.05% Digitalis	0.025% Yoh. + 0.0345% Digitalis	0.025% Yoh. + 0.025% Digitalis
223	204	180

ments Using Digitalis (C)

79	270	271	272
25% h. + 011% Gluc.	0.025% Yoh. + 0.00066% Dig. Gluc.	0.025% Yoh. + 0.00033% Dig. Gluc.	0.025% Yoh. + 0.000165% Dig. Gluc.
52	240	220	199

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

The Identity of an Antibacterial Factor in the Saliva of Certain Mammalia. S. L. Rosenthal, W. M. McNabb and R. C. Snyder. *J. A. D. A. 26,* 1859 (1939). Attempts to induce oral Vincent's infection in normal animals by inoculation have been unsuccessful. While localized infection has resulted in some cases it is not comparable with the disease in man. The lesions heal spontaneously and the infection is not transmitted to other animals in contact with the affected animals.

An investigation of this apparent immunity was begun by bacteriologic examination of the mouths of normal mammals including both domesticated and wild animals. Smears were notable for their low bacterial count in comparison with man's and for the complete absence of motile microorganisms. Fusiform bacilli or spirochetes similar to those found commonly in the human oral cavity were not found except in a few cases where some pathologic condition or an extremely dirty mouth existed.

Apparently, the mouths of healthy animals contained antibacterial substances since their habits and diets must bring them in contact with innumerable spirochetal forms yet not only is spirochetosis rare in these species but also the spirochete is seldom seen in healthy specimens.

In an attempt to identify such a substance saliva was collected from several animals of different species. The pH was found to be from 8.4 to 8.6. Each sample was subjected to the motility test which consists in bringing a definite quantity of the fluid under a dark field microscope with an equal quantity of saliva from a patient with Vincent's infection. The saliva contains actively motile spirochetes, vibrios and bacilli together with the natural organic débris. The antibacterial properties are measured by the time elapsing from the moment of contact of the solutions to cessation of movements of (1) spirochetes, (2) vibrios and (3) motile bacilli. Other workers have shown that loss of motility in *T. pallidum* entails loss of pathogenicity.

Contact with all normal animal saliva caused spirochetes and vibrios from a human mouth to lose motility instantly. Many instantly destroyed the motility of all bacilli as well but others failed to penetrate débris well or to stop the movement of all motile bacilli.

The pH of saliva from dogs which were household pets and suffering from Vincent's infection was found to be 6.7-7.6, about the range of that in normal man. These animals upon recovery were found to have a salivary pH of 8.6 and all had regained the inhibitory effect on the motile oral flora.

The constituent of normal animal saliva which possessed this antibacterial action was finally found to be sodium carbonate. Interesting was the additional finding that not in pH alone does the effect of sodium carbonate rest, since a solution of sodium hydroxide of similar pH is much less active.

Chemical tests were made on two dogs and five persons with acute Vincent's infections. Continuous topical applications of a molar solution of sodium carbonate were made to the dried gingival tissues for fifteen minutes. Home care was limited to hourly rinsing or topical applications with this solution. Resolution was rapid in all cases.

L. F. T.

Methyl Cellulose in Pharmacy. G. A. Bergy, *Amer. Prof. Pharm.* (V, 691 (1939)). Methyl cellulose dissolved in distilled water at normal temperatures forms a stable jelly. This property enables its use with simple procedures, to form mucilages resistant to extreme heat, cold and light and impervious to bacterial decomposition. Preservatives needed are merely to protect the other ingredients of the preparation.

Methyl cellulose is marketed as a coarse, dry fibrous mass which when dissolved in water produces a uniformly viscous product free from lumps.

A slight sediment may form on standing and may be removed by centrifugalization or decantation of the supernatant liquid.

Solutions of methyl cellulose are neutral in reaction, exhibiting excellent dispersing and emulsifying qualities. Emulsions made thus are strongly alkaline in hot or cold, and on cooling the clarity and thickness are improved. This is advantageous in preparations containing titanium dioxide, zinc stearate or carbon black for the shearing

effect of mechanical agitation advances and improves reduction of particle size.

The solutions of methyl cellulose are prepared by pouring 10 to 15 parts of boiling water over 1 part of the substance, stirring thoroughly until the mass swells and lumps dissolve, being careful not to incorporate too much air. Allow the solution to cool to approximately 60° C., stir, and cool completely, stirring again to make it homogeneous. Strain through unsized, unbleached muslin. The stock solution thus prepared may be diluted to any desired strength.

Solutions of methyl cellulose and products containing them are harmless to man and animals either internally or externally. Being resistant to marked changes in pH, the stomach's acidity and the intestines alkalinity do not decompose it.

The author suggests the use of methyl cellulose as a thickening or binding agent, and emulsifying or dispersing agent in pharmaceutical or dermatological preparations. Use the rule for tragacanth of seventy grains to the pint or 10 gms. to the liter for the strength to be employed. The use of methyl cellulose in dentifrices, skin creams, depilatories, hair grooms, cleansing creams and dermal creams with a typical formula for each is recommended.

M. H.

Sulfapyridine for Pneumonia Control. *Baltimore Health News, 16,* 172 (1939) through *Squibb Abstr. Bull. 12,* 1303 (1939). Sulfapyridine has been used extensively in the treatment of pneumonia in a number of hospitals in Baltimore with great reduction in mortality. In one large series of cases only 7 per cent. mortality occurred and in a series of 70 small children with measles and pneumonia none died. Sulfapyridine is more effective than antipneumococcic serum and therefore it will probably be more generally used in the treatment of pneumonia in the patients' home. It was recommended by the Pneumonia Control Committee of the Maryland State Board of Health as the chief therapeutic agent in the control of this disease. This does not mean that the use of serum should be discarded but rather that serum be used as a supplement especially in very severe cases and in those not promptly improved by sulfapyridine. It is suggested that sulfapyridine be employed also in the treatment of lobar and interstitial pneumonia. Careful check-up must be main-

tained against toxic reactions. It should be discontinued at once if the white blood cell count falls below 4, 500/cu. mm. with less than 50 per cent. polymorphonuclear leukocytes.

It should also be withdrawn if a hemoglobin fall of 30 per cent. or more is observed, if there is any clinical evidence of excessive hemolysis or if more than a very few red blood cells are found in the urine. Urinary precipitation of acetylsulfapyridine is less likely to occur if sodium bicarbonate and moderately large amounts of fluid are given. L. F. T.

Deflagration with Sodium Peroxide as a Simple Analytical Process for the Determination of Halogen, Sulfur and Other Constituents in Organic Substances. R. Kraus. *Z. Anal. Chem. 117,* 243 (1939) through *Squibb Abstr. Bull. 12,* 1402 (1939). Deflagration of solid organic substances and certain liquids by quick and short heating with a large excess of Na_2O_2 in a covered nickel crucible by the method presented gives a quick and complete combustion with relatively little attack on the crucible. The determination of halogens, sulfur and phosphorus may then be accurately made. Viscous liquids are first mixed with MgO and liquids of high boiling point are absorbed in filter paper in the crucible before mixing with the Na_2O_2. The method is limited for low percentage of Cl, S.. etc., only by the "blank" of the Na_2O_2. It is applicable to substances, such as chlorotoluidine, which are not readily decomposed by the Carius method. The method is particularly well suited for routine analysis.

L. F. T.

An Experimental Study of the Relation Between Concentration of Disinfectants and Time Required for Disinfection. F. W. Tilley. *J. of Bacteriology* (*38,* 499, 1939, No. 5). Different types of disinfectants act upon bacterial protoplasm in different ways. It can not be expected that the relation between concentration of disinfectant, and time required for disinfection can be expressed by a single formula applicable to all types. These factors do appear to be exponentially related over considerable ranges of concentrations and disinfection times in many disinfectants. In such cases the derived mathematical values may be useful in evaluating or predicting bactericidal efficiency.

The only variables allowable are: Concentration of disinfectant and time required for disinfection. The value n is known as the "concentration exponent" or "coefficient of dilution," denoting the degree to which dilution lessens the rate of disinfection. As an example, ethyl alcohol has a high value of n but loses its efficiency on dilution more rapidly than phenol which has an n value of about one half.

A modified Rideal-Walker technic was used to determine the bactericidal efficiencies of phenol, orthocresol, paracresol, orthobutylphenol, parabutylphenol, resorcinol, n-propylresorcinol, ethyl alcohol and n-butyl alcohol against *Staphylococcus aureus* and *Eberthella typhosa*. The following formula was employed to calculate n:

$$n = \frac{\log t_2 - \log t_1}{\log C_1 - \log C_2}$$

TABLE 4

Values of n determined at different temperatures

Disinfectant	Test Organism	10° C.	20° C.	30° C.	40° C.
Phenol	*E. typhosa*	7.9	7.5	5.9	5.2
	S. aureus	6.5	6.5	6.4	5.4
Orthocresol	*E. typhosa*	8.3	7.9	5.5	5.1
	S. aureus	7.8	7.6	8.1	6.8
Paracresol	*E. typhosa*	8.9	8.4	6.4	5.3
	S. aureus	8.2	8.7	9.4	7.0
O-Butylphenol	*E. typhosa*		9.2	7.2	
	S. aureus		8.5	9.1	
P-Butylphenol	*E. typhosa*		9.2	9.3	
	S. aureus		8.9	8.1	
Resorcinol	*E. typhosa*	4.6	5.1	5.2	
	S. aureus	4.4	5.0	6.2	
Ethyl alcohol	*E. typhosa*	12.7	11.4	8.8	
	S. aureus	11.4	11.1	8.5	
N Butyl alcohol	*E. typhosa*		11.9	10.3	
	S. aureus		11.8	10.1	

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D., F. R. S. A.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

When an ungiving ash tray falls on a mahogany table it usually leaves its tell-tale mark. Such indentations, if they are not too deep, can usually be removed without difficulty by a paste of glycerin, water and iron oxide. Dip a hard felt pad in the paste and rub briskly back and forth over the scratched surface until the markings have disappeared. This procedure is especially adapted to removing shallow scratches. Deep gougings, however, require more specialized treatment. Many polishing materials used in mechanical methods utilize glycerin as an essential ingredient.

And speaking of glycerin, a commodity much more useful than most people know. Christmas decorators will do well to remember that soaking holly wreaths and similar fresh greenery in a 5 per cent. solution of glycerin in water keeps these Yuletide ornaments sprightlier and livelier than they might otherwise keep. Of course after the pre-soaking the hung-up wreaths, etc., should be allowed to drain thoroughly before being placed. This procedure is necessary only in the case of leaves and leaf or other live green ornaments used for interior decorations. Outside weather takes care of its own, but the warmth inside crisps too soon the cold loving evergreens.

If you want to transfer a favorite design or print on a news-sheet to paper, cloth, wood or other surfaces, this can usually be satisfactorily accomplished by employing the following simple solution of familiar ingredients:

Glycerin	1½
Soap	4
Alcohol	10
Water	10

Wet thoroughly the print or drawing to be transferred. Remove excess liquid with a clean blotter and invert print onto the paper or cloth to which it is to be transferred. Lay a piece of paper over it and rub with a blunt article such as a knife handle.

The intimate chemical relationships existings between alkaloids, hormones and many dyestuffs are not always appreciated by pharmacologists. Many of the new synthetics also are first cousins to the coal tar dyestuffs. For instance, Sulfanilamide compounds, used in the war against disease on a score of fronts, promise to be useful in the scientific study of the undiseased tissues of animals and plants. One such has been found to be an effective "vital stain." Vital stains are dyes used on living tissues, which they color up and thus make easier to examine under the microscope. The sulfanilamide compound used has been long since known under the trade name of Neoprontosil, and it tinges the cells of plants and insects red. The discovery was made incidentally, while investigating possible effects on virus diseases.

Any new use for castor oil to divert it from the use that you think of when you hear the name is news. Castor oil is being used to make paint, replacing the tung oil largely imported from China and now difficult to get on account of the Japanese invasion. As pressed from the castor bean, the oil will not dry properly. So it is necessary to dehydroxylate it, snatch out some hydrogen and oxygen (water, if you must know) atoms from its molecule, which makes it a drying, odorless, non-yellowing, oil comparable with tung oil. It is a 9-11 octadecadieneic acid, if you talk chemistry; Dehydrol, if you talk paint manufacture. As a partner to the dehydrated castor oil, there is phenol resin, one of the most familiar synthetic plastics made from carbolic acid (phenol) and formaldehyde, modified into a pale, extra hard resin for making quick drying, water resistant varnishes, enamels and undercoats.

Wounds in plants are caused to heal by an acid which has been isolated in crystalline form by Drs. James English, Jr., James Bonner and A. J. Haagen-Smit of the California Institute of Technology,

and for which they propose the name "traumatic acid." The substance has the chemical formula $C_{12}H_{22}O_4$, and is identical with the organic acid, 1-decene-1, 10-dicarboxylic acid. The three experimenters, using a solution of this acid synthetically prepared, induced rapid formation of healing tissue on the cut surfaces of potato tubers. The discovery of the chemical nature of the wound hormone is announced briefly in "Science," with the statement that a more detailed report will be published later, when its application to animal wounds may be discussed.

A chemical compound that may prove as good a remedy against infectious diseases as sulfanilamide, with less toxic effects, is announced by the U. S. Public Health Service.

The compound, prepared by Drs. Hugo Bauer and Sanford M. Rosenthal, at the National Institute of Health, contains phosphorus instead of sulfur, and is different in other ways from sulfanilamide. Three such compounds have been prepared, of which one, bis (4-dimethylaminophenyl) phosphinous acid, checked streptococcus infections in mice and had a low toxicity.

No human trials of these chemicals have been made yet, nor will they be, Dr. Rosenthal said, before more extensive laboratory investigations.

The object of the research, in which compounds with arsenic substituting for the sulfur of sulfanilamide were also made, is to find chemicals which either are better than sulfanilamide or are effective against germ infections which sulfanilamide does not check.

Listerine has listened to the law! Thousands who have hearkened to the outrageous claims made by its manufacturers and who have sought through it some surcease from the dandruff distribution will find little comfort in the fact that the Lambert Pharmacal Company have entered into a stipulation with the Federal Trade Commission to cease making the following unwarranted advertising claims for this product:

(1) That all dandruff is due to an infection with Pityrosporon ovale or any other organism;

(2) That dandruff necessarily is a germ disease;

(3) That the dandruff germ has been isolated or identified;

(4) That the presence of Pityrosporon ovale necessarily means dandruff or that with its destruction dandruff disappears;

(5) That dandruff is necessarily infectious, contagious or "catching" or is in all instances passed from one person to another, or

(6) That any of the foregoing assertions is a "scientific fact" or a "fact definitely established by scientists."

It was also stipulated that the company stop representing that the product either cures or permanently relieves dandruff; that the product "kills the dandruff germ," "attacks the cause of dandruff," or penetrates infected hair follicles, or "annihilates" the dandruff germ.

Finally, the company will no longer advertise: that the product has "marked curative properties due to certain ingredients in a unique combination shared by no other antiseptic"; that ordinary remedies "aren't even antiseptic," are "smelly," affect only surface symptoms, or merely remove surface symptoms temporarily, or that competitive products are obviously inferior to "Listerine Antiseptic" as a remedy for dandruff—when such are not the facts.

But despite these capitulations there still seems to be a demand for Listerine if only because of its name.

BOOK REVIEWS

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

A Textbook of Materia Medica, Pharmacology and Therapeutics. By Harold N. Wright, M.S., Ph.D., Associate Professor of Pharmacology, University of Minnesota; and Mildred Montag, R.N., M.A., Instructor in Nursing Arts, St. Luke's Hospital, New York City. 566 pages with 83 illustrations. Philadelphia and London: W. B. Saunders Company, 1939. Cloth, $2.75.

This book is obviously intended to be used by pupil nurses, as is shown both by the subjects covered and the method of presentation. The first seventy-five pages are given over to an outline of some points of elementary pharmacy which are of interest to the nursing profession; then follows about fifteen pages chiefly devoted to consideration of various methods of administering drugs. This leaves about four hundred pages to be devoted to the subject of pharmacology. Even in this latter part of the book the authors have in mind always their intended audience and continuously emphasize those pharmacological facts which especially concern the nursing profession, with a compensatory skimping of many of the phases which are of interest to pharmacists.

The pharmacological portion of the book displays a pleasing clarity of style which is enhanced by a number of illustrative diagrams but is unfortunately marred by weird typographical arrangement. Here and there the effort at simplicity has lured the author into some generalizations which are not strictly accurate—such as the implication that all germicides act by precipitating protein—but anyone who can read the book unperturbed by the inconsistencies in the use of black-face type and in the paragraphing should obtain an understanding of the modern ideas of drug action. The drugs considered are not limited to those official but include a considerable number of the more important of the proprietary synthetics.

H. C. Wood.

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TITLE AND SUBJECT INDEX FOR 1939

(A)—Abstract
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Doctor says, "Come right in."

WE PAY HIM, BUT HE WORKS FOR YOU

● **Receptionists in busy offices everywhere, welcome the Lilly man. Even though the doctor must be selective in his interviews, he wants to see the Lilly man, who through a sense of responsibility engendered by the experience of a long line of forebears, knows how to conserve the physician's time as well as his own.**

Every successful interview conducted by the Lilly man in your territory means more prescriptions for your store. Every additional prescription means more profit at the end of the year. The Lilly man works diligently in your behalf every working day in the year, yet his services cost you nothing. Maintain adequate stocks. No man ever loses on a Lilly Product.

John S. Rowe completed his thirty-fourth year as a Lilly representative last October 1. Except for a brief period in western Maryland, the entire thirty-four years have been spent in North Carolina. Loved and respected by all who know him, Mr. Rowe now serves the drug trade in and around Hickory.

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